

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claims 1-81 (canceled)

Claim 82. (currently amended) A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

(a) hybridizing a sample comprising the target nucleic acid to an array of oligonucleotide probes immobilized on a solid support, the array comprising:

(1) a first probe set comprising a plurality of different probes, each probe exactly complementary to a subsequence of the reference sequence, the probe including a single interrogation position complementary to a corresponding nucleotide in the reference sequence, wherein the reference sequence is at least 50 bases, and the different probes of the first probe set are overlapping probes spanning the reference sequence;

(2) a second probe set comprising a corresponding probe for each of the different probes in the first probe set, the corresponding probe in the second probe set being identical to the corresponding probe from the first probe set that includes the interrogation position, except that the one interrogation position is occupied by a different nucleotide in each of the two corresponding probes from the first and second probe sets;

wherein, the different probes in the first probe set have at least three interrogation positions respectively corresponding to each of at least three contiguous nucleotides in the reference sequence, and

(b) detecting a hybridization pattern of the oligonucleotide probes to the target nucleic acid and determining from the hybridization pattern whether a nucleotide in the target sequence is the same or different from the corresponding nucleotide in the reference sequence.

Claim 83. (previously presented) The method of claim 82, wherein the determining comprises comparing the hybridization pattern to the target nucleic acid with a hybridization pattern of a nucleic acid having the reference sequence to the array of oligonucleotide probes.

Claim 84. (previously presented) The method of claim 82, wherein the determining step comprises:

- (1) comparing the relative specific binding of two corresponding probes from the first and second probe sets;
- (2) assigning a nucleotide in the target sequence as the complement of the interrogation position of the probe having the greater specific binding;
- (3) repeating (1) and (2) until each nucleotide of interest in the target sequence has been assigned.

Claim 85. (currently amended) A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

- (a) hybridizing a sample comprising the target nucleic acid to an array of oligonucleotide probes immobilized on a solid support, the array comprising:
 - (1) a first probe set comprising a plurality of different probes, each probe exactly complementary to a subsequence of the reference sequence, the probe including a single interrogation position complementary to a corresponding nucleotide in the reference sequence,
 - (2) second, third and fourth probe sets, each comprising a corresponding probe for each of the different probes in the first probe set, the corresponding probes in the second, third and fourth probe sets being identical to the corresponding probe from the first probe set that includes the interrogation position, except that the interrogation position is

occupied by a different nucleotide in each of the four corresponding probes from the first, second, third and fourth probe sets;

wherein, the different probes in the first probe set have at least three interrogation positions respectively corresponding to each of at least three contiguous nucleotides in the reference sequence, and

(b) detecting a hybridization pattern of the oligonucleotide probes to the target nucleic acid and determining from the hybridization pattern whether a nucleotide in the target sequence is the same or different from the corresponding nucleotide in the reference sequence.

Claim 86. (previously presented) The method of claim 85, wherein the determining comprises comparing the hybridization pattern of the target nucleic acid with a hybridization pattern of a nucleic acid having the reference sequence to the oligonucleotide probes.

Claim 87. (previously presented) The method of claim 85, wherein the determining comprises:

- (1) comparing the relative specific binding of four corresponding probes from the first, second, third and fourth probe sets;
- (2) assigning a nucleotide in the target sequence as the complement of the interrogation position of the probe having the greatest specific binding;
- (3) repeating (1) and (2) until each nucleotide of interest in the target sequence has been assigned.

Claim 88. (previously presented) A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

- (a) hybridizing the target nucleic acid to an array of oligonucleotide probes immobilized on a solid support, the array comprising:

a perfectly matched probe exactly complementary to a subsequence of a reference sequence, the perfectly matched probe having a plurality of interrogation positions respectively corresponding to a plurality of nucleotides in the reference sequence,

for each interrogation position, three mismatched probes, each identical to the perfectly matched probe including the plurality of interrogation positions, except in the interrogation position, which is occupied by a different nucleotide in each of the three mismatched probes and the perfectly matched probe;

(b) for each interrogation position,

(1) comparing the relative specific binding of the three mismatched probes and the perfectly matched probe;

(2) assigning a nucleotide in the target sequence as the complement of the interrogation position of the probe having the greatest specific binding.

Claim 89. (previously presented) The method of claim 88, wherein the target sequence has an undetermined substitution relative to the reference sequence, and the method assigns a nucleotide to the substitution.

Claim 90. (currently amended) A method of comparing a target nucleic acid with a reference sequence comprising a predetermined sequence of nucleotides, the method comprising:

hybridizing the target sequence to an array of oligonucleotide probes immobilized on a solid support, the array comprising at least one pair of first and second probe groups, each group comprising a first and second sets of oligonucleotide probes,

the first probe set comprising a plurality of different probes, each probe exactly complementary to a subsequence of a reference sequence, the segment including a single interrogation position complementary to a corresponding nucleotide in the reference sequence, wherein the reference sequence is at least 50 bases, and the different probes of the first probe set are overlapping probes spanning the reference sequence;

the second probe set comprising a corresponding probe for each of the different probes in the first probe set, the corresponding probe in the second probe set being identical to the corresponding probe from the first probe set, except that the interrogation position is occupied by a different nucleotide in each of the two corresponding probes from the first and second probe sets;

wherein the probes in the first probe set have at least three interrogation positions respectively corresponding to each of three contiguous nucleotides in the reference sequence;

wherein each of the different probes in the first probe set from the first group is exactly complementary to a subsequence of a first reference sequence and each of the different probes in the first probe set from the second group is exactly complementary to a subsequence from a second reference sequence;

determining which probes in the first group, relative to one another, hybridize to the target sequence, the relative specific binding of the probes indicating whether the target sequence is the same or different from the first reference sequence;

determining which probes in the second group, relative to one another, hybridize to the target sequence, the relative specific binding of the probes indicating whether the target sequence is the same or different from the second reference sequence.

Claim 91. (previously presented) The method of claim 90, wherein the hybridizing step comprising hybridizing the target sequence and a second target sequence to the array, and the relative specific binding of the probes from the first group indicates that the target is identical to the first reference sequence, and the relative specific binding of the probes from the second group indicates that the second target sequence is identical to the second reference sequence.

Claim 92. (previously presented) The method of claim 90, wherein the first and second target sequences are heterozygous alleles.

Claim 93. (previously presented) The method of claim 82, wherein the probes are 6-30 nucleotides long.

Appl. No. 09/510,378

PATENT

Amdt. dated September 2, 2004

Amendment under 37 CFR 1.116 Expedited Procedure

Examining Group

Claim 94. (previously presented) The method of claim 90, wherein the probes are 6-30 nucleotides long.